UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/263,626	03/05/99	MOORE P	PF466

HM12/0829

HUMAN GEMONE SCIENCES
9410 KEY WEST AVENUE
ROCKVILLE MD 20850

EXAMINER	
BRANNOCK,M	
ART UNIT	**PAPER NUMBER**
1646	11

DATE MAILED: 08/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/263,626	P.A. Moore et al.
Examiner	**Group Art Unit**
Michael Brannock, Ph.D.	1646

☒ Responsive to communication(s) filed on *Jun 2, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *25-99* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *25-99* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of Application: Claims and Amendments

1. Applicant is notified that the amendments put forth in Paper 10, 6/12/00, have been entered in full. It is made of record that page 6 of Paper 10 was missing. Applicant supplied a copy of page 6 which has been subsequently entered.

2. Claims 25-99 are pending and under examination.

Response to Amendment

Priority:

3. In item 6 of Paper 6, 1/3/00, the examiner raised the issue that no basis for priority is found in US 60/078563 for SEQ ID NO: 1 and 2 nor for ATCC deposit number 209691. Applicant argues that SEQ ID NO: 1 and 2 correspond to SEQ ID NOs: 11 and 21 of 60/078563 with the exception of a few minor sequencing errors such misidentified nucleotides, insertions, or deletions, some of which cause frame shifts in the reading frame of the predicted amino acid sequences. Further, Applicant argues that SEQ ID NO: 1 and 2 of the instant application and SEQ ID NOs: 11 and 21 of 60/078563 are derived from the same clone, namely HTAEK 53, having a deposit number of 209641, and that therefore priority to SEQ ID NO: 1 and 2 should be given the filing date of the 60/078563 application. This argument has been fully considered but not deemed persuasive because, having the 60/078563 application as a guide, one of skill in the art would not be in possession of SEQ ID NO: 1 or 2, and would have wrongly used SEQ ID

NOs: 11 and 21 - as was taught by the 60/078563 application. However, claims directed solely to deposit number of 209641 would be enabled by the 60/078563 application, and will therefore be given the priority date of the filing date of the 60/078563 application.

Withdrawn Objections/Rejections:

4. The objection to the disclosure, as put forth in item 7 of paper 6 is withdrawn in view of Applicant's amendments which put forth the intended purpose of the table on pages 115-119.

5. The rejection of claims 25-34, 37-40 and 42-50 under USC 112, first paragraph, for lacking enablement commensurate in scope with that of the claims is withdrawn in view of the subsequent finding that the claims lack enablement for a specific or otherwise substantial utility (see below).

6. The rejected of claims 51-59 under 35 U.S.C. 112, first paragraph, as put forth in item 12 of Paper 6 is rendered moot due to Applicant's cancellation of the claims.

Maintained rejections:

7. Claims 37-40 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons put forth in item 9 of Paper 6 and reiterated below.

Claim 37(a) recites a polynucleotide encoding a polypeptide comprising amino acids m-371, wherein m is an integer. It is unclear whether applicant intends the term " m-371" to designate a range, i.e. from integer m ***to*** 371, or if the applicant intends the term to designate an arithmetic expression, i.e. integer m ***minus*** 371. This ambiguity is also true for 37(b) and (c) and for claims 38-40 which depend on claim 37.

Applicant argues that the term "m-371" is intended to denote a range (see page 7 of paper 10), however, in order to overcome the rejection, this fact must be incorporated into the language of the claim.

8. Claim 37 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by GenEmbl accession number X91553 for the reasons put forth in item 14 of Paper 6 regarding claim 36-38, and reiterated below. Claims 36-38 claim a nucleic acid that hybridizes to a polynucleotide of SEQ ID NO: 1 (claim 36) or encoding a polypeptide comprising at least one amino acid residue of SEQ ID NO: 2 (claims 37c and 38). GenEmbl accession number X91553 discloses a polynucleotide that is 100% identical to SEQ ID NO: 1 over the range of positions 778-806, and would therefore hybridize to SEQ ID NO: 1 under highly stringent conditions and would also be expected to encode a polypeptide having a sequence identical to positions 256-264 of SEQ ID NO: 2.

Applicant argues that the rejection of claim 36 is obviated due to Applicant's amendment of the claim to recite "wherein said polynucleotide is not Genbank Accession No. X91553". The

examiner agrees, however, as put forth above, GenEmbl accession number X91553 discloses a polynucleotide that is 100% identical to SEQ ID NO: 1 over the range of positions 778-806, and would therefore hybridize to SEQ ID NO: 1 under highly stringent conditions and *would also be expected to encode a polypeptide having a sequence identical to positions 256-264 of SEQ ID NO: 2.* Thus, claims 37 and 38 are still encompassed by the rejection.

New Rejections:

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25-99 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Claims 25-99 are directed to polynucleotides of SEQ ID NO: 1 encoding a polypeptide of SEQ ID NO: 2. The instant specification puts forth that the polypeptide is useful in a method to determine what the physiological effects of the polypeptide might be (see page 55, beginning at line 31). This proposed use lacks a specific and substantial utility. It is not a specific use because any protein derived from natural sources could be used in exactly the same way. Further, many polynucleotides are known in the art to encode polypeptides, yet the polypeptides have no known

function or known ligands. Any of these orphan clones could be used in the manner described in the specification for the claimed polynucleotide.

Furthermore, the proposed use of the polypeptide to screen for biologic effects of the polypeptide is not a substantial utility. A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of treating an unspecified disease or condition with a material that has no particular correlation with a disease would not constitute a substantial utility. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

The specification puts forth that the polypeptides may be useful in treating or detecting deficiencies or disorders of hematopoeitic cells, such disorders including HIV, Digeorge Syndrome, ataxia telangiectasia, phagocyte bactericidal dysfunction, etc. (see page 56, third paragraph). A stated belief that a correlation exists between the polypeptides and any number of diseases is not sufficient guidance to use the claimed polynucleotides to treat and/or diagnosis a particular disease; it merely defines a starting point for further research and investigation.

The specification puts forth that polypeptides of the instant invention are expressed in HeLa cells, activated T cells, AF49 Cells, spleen, and lymph - and have a pattern consistent with

immune specific expression (see page 7, L15). Further Applicant argues in Paper 10, page 8, that the polynucleotides and polypeptides can be used as a tissue specific marker. However, consistent with current examination guidelines, the proposed use as a tissue specific marker or chromosomal marker does not constitute a substantial utility. Almost all polynucleotides and polypeptides have some tissue specific pattern of expression, but absent some guidance as to a correlation between the pattern and some disease state or other useful feature, one of skill in the art would not be able to use the polypeptides other than as a starting point for further research and investigation into any practical uses for the polynucleotides and polypeptides - if indeed any can be found.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids.

10. Claims 25-60 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Furthermore, the claims encompass polypeptide variants of the polypeptide of SEQ ID NO: 2, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 2;

should Applicant establish a specific and substantial utility for the claimed polynucleotides, Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 2, but which still retain a desired property of the polypeptide of SEQ ID NO: 2.

The specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, the Applicant has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 2 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 2 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 2 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 2, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 2.

Applicant argues on page 12 of Paper 10 that the specification teaches which residues comprise the epitope bearing portions of the protein corresponding to SEQ ID NO: 2 and also how to determine which amino acid changes are phenotypically silent and how to determine which amino acids of the protein are essential to its function. This argument has been fully considered but not deemed persuasive because, primarily, the specification has not disclosed

what the function of the polypeptide is. Thus, one of skill in the art would first have to determine a function of the polypeptide - and this burden amounts to a starting point for further research. Second, the claims encompass an almost infinite number of amino acid changes in the polypeptide of SEQ ID NO: 2, and the requirement of identifying which changes would preserve function, if a function were known, or of identifying which amino acid changes would impart any desired property, if such a property were known, would place an undue burden of experimentation on one highly skilled in the art.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2; Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure, pp. 14-16). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art

to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to generate the infinite number of amino acid sequence variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Fridays from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

MB

August 21, 2000